REMARKS/ARGUMENTS

The Pending Claims

Claims 1-5, 7-10, 12, 13, 16-22, and 40 are pending and are directed to a method of inducing an immunological response.

Summary of the Office Action

The Office rejects claims 1-5, 7-10, 12, 13, 16, and 40 under 35 U.S.C. § 103(a) as allegedly obvious over Schlom et al. (WO 00/34494) and Pecher (WO 01/24832).

The Office rejects claims 17-22 under 35 U.S.C. § 103(a) as allegedly obvious over Schlom et al. (WO 00/34494), Pecher (WO 01/24832), and Grosenbach et al., *Cancer Research, 61*: 4497-4505 (2001).

These rejections are traversed for the following reasons.

Discussion of the Obviousness Rejections

In response to Applicants' arguments, the Office maintains that the subject matter of the pending claims is obvious in view of the Schlom and Pecher references when considered alone or in further combination with the Grosenbach reference. The obviousness rejections are traversed for the following reasons.

The present invention, as defined by the pending claims, is directed to a method for inducing an immunological response against a cell expressing a breast cancer associated antigen in a human, wherein the method comprises (a) selecting a human having breast cancer or at risk for developing such a breast cancer tumor, (b) administering to the individual a first poxvirus vector containing one or more DNA segments that encode (i) mucin (MUC) or an antigenic portion thereof or modified version thereof and (ii) carcinoembryonic antigen (CEA) or an antigenic portion thereof or modified version thereof, and (c) at regular intervals thereafter administering at least a second poxvirus vector containing one or more DNA segments that encode (i) MUC or antigenic portion thereof or modified version thereof and (ii) CEA or an antigenic portion thereof or modified version

thereof, such that an immunological response against the cell expressing the breast cancer associated antigen is induced in the individual.

The Office contends that the Schlom reference teaches the administration of more than one dose of recombinant poxvirus encoding a tumor antigen, such as MUC or CEA, or a prime-boost delivery method where a first vector is administered followed by administration of a second vector, wherein the first and second vectors are different strains of poxvirus. The Office further contends that the Schlom reference discloses that poxvirus vectors can encode more than one tumor associated antigen, as well as costimulatory molecules. Therefore, the Office contends that the only missing element from the Schlom reference is a specific teaching to choose MUC and CEA as the tumor associate antigens to express together in a recombinant virus vector.

The Office contends that the Pecher reference supplements the Schlom reference by teaching the combined administration of vectors, including vaccinia virus vectors, encoding MUC1 or CEA to patients for the treatment of tumors. The Office acknowledges that the Pecher reference does not disclose a single vector encoding MUC and CEA, as required by the pending claims. However, the Office contends that the Pecher reference provides the motivation to use MUC1 and CEA as the more than one tumor associated antigen in the vectors of the Schlom reference.

The Office relies on the disclosure of the Grosenbach reference to address the additional limitations recited in claims 17-22 regarding the particulars of the prime-boost protocol.

While the Schlom reference indicates that poxvirus vector can encode more than one tumor associated antigen, the Schlom reference does not disclose a poxvirus vector encoding MUC and CEA or a prime-boost protocol employing two poxvirus vectors encoding MUC and CEA, as required by the pending claims. Although the Pecher reference discloses a composition comprising a vector (e.g., plasmid) encoding MUC1 and a vector (e.g., plasmid) encoding CEA, the Pecher reference does not disclose any working examples wherein the vectors are administered together. Instead, the Pecher reference describes an experiment wherein an adenovirus vector encoding MUC1 is administered to a mouse followed by administration 14 days later of a plasmid encoding MUC1. In other words, in the experiment

of the Pecher reference, a vector encoding only one tumor associated antigen (MUC) was used. Similarly, the Grosenbach reference discloses administration of only one tumor associated antigen (CEA), which is in combination with costimulatory molecules (TRICOM).

As discussed in the previous replies to Office Actions, the prior art discloses that the presentation of two antigens together (at the same location) was thought to result in competition between the two antigens with one antigen being dominant, thereby resulting in a reduced immune response to one or both of the antigens (see, e.g., page 4397, second column, fourth full paragraph, of Palmowski et al. (*J. Immunol., 168*: 4391-4398 (2002); of record), and page 83, lines 1-3, of Brody et al. (*Immunol., 22*: 75-85 (1972); of record). For this reason, one of ordinary skill in the art would not have been motivated to prepare a vector encoding the two tumor associated antigens of MUC and CEA, as required by the pending claims. As noted above, while the Pecher reference alleges that individual vectors comprising MUC or CEA could be administered together as a cancer vaccine, the Pecher reference does not disclose any evidence (e.g., a working example) of the efficacy of such a method. Therefore, one of ordinary skill in the art would not have found that the teachings of the Pecher reference were sufficient to supersede the above-described teachings of the prior art regarding antigen competition.

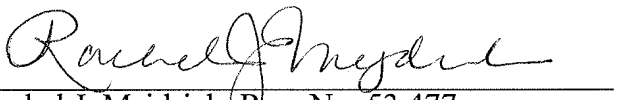
As noted previously, the inventors surprisingly discovered that the inventive methods that employ a vector encoding CEA and MUC result in the beneficial effect of stimulating the immune system to target against both the CEA and MUC-1 antigens. In particular, the specification describes a Phase I clinical trial, which established the preliminary safety and efficacy profiles of targeted cancer immunotherapy using a prime-boost protocol in cancer patients (see, e.g., paragraphs 258-274). The post-filing Gulley (*Clin. Cancer Res., 14(10)*: 3060-3069 (2008); of record) and Tsang (*Clin. Cancer Res., 11*: 1597-1607 (2005); of record) references confirm the efficacy of the inventive methods. In particular, the Gulley and Tsang references demonstrate that the inventive methods result in the development of a significant increase in antigen-specific (MUC and CEA) immune response (see, e.g., Abstracts of the Gulley and Tsang references) and evidence of a clinical benefit (see, e.g., Abstract of the Gulley reference).

The benefits attendant the present invention are unexpected and surprising in view of the teachings in the prior art at the earliest priority date of the application (e.g., the Palmowski and Brody references). Accordingly, the subject matter of the pending clams would not have been obvious to one of ordinary skill in the art at the relevant time in view of the combined disclosures of two or more of the Schlom, Pecher references, and Grosenbach references . For the above-described reasons, the obviousness rejections should be withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,



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